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10/031,532	05/02/2002	Harry B. Gray	CIIT1490-3	6210

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,532	GRAY ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38-47* is/are allowed.

6)☒ Claim(s) *20-35,37 and 46* is/are rejected.

7)☒ Claim(s) *36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 03 August 2005 is acknowledged and has been entered.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56.

Claim Objections

3. Claim 46 is objected to because of the following informalities: it seems as if the instant claim should be dependent on claim 38, since the exact limitation is already claimed as dependent on claim 20 in currently amended claim 33. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide support for the newly added limitation "selecting the identifying agent based on the modulating capacity of each of the candidate agents" (lines 13-14). The newly added limitation is therefore considered to be new matter.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 37 recites the limitation "the identifying agent" in line13. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 20-22, 26, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401).

Ullman et al reference teaches the steps of performing an assay by providing a medium suspected of containing an analyte (i.e. target biomolecule), a photosensitizer associated with a specific binding partner member (i.e. substrate molecule; forming a complex), and a suspendible particle comprising a chemiluminescent compound that, when treated with light in combination with the photosensitizer (i.e. irradiating the complex), produces luminescence related to the amount of analyte in the medium (i.e. determining the presence of the complex by the signal emitted by the photosensitizer). See column 34, line 65 to column 35, line 14.

However, Ullman et al fail to teach the step of characterizing the target biomolecule by optically analyzing the same to determine the structural properties thereof.

Fesik et al reference teaches determining the structure of a complex between a target molecule and ligands by x-ray crystallography, in order to determine the spatial orientation of ligands relative to the target molecule for screening purposes.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al with the step of determining the structure of a complex between a target molecule and ligands by x-ray crystallography, as taught by Fesik et al, for the expected benefit of determining the spatial orientation of ligands relative to the target molecule for screening purposes. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of performing x-ray crystallography on a target-ligand complex, as taught by Fesik et al, in the method of Ullman et al, since Ullman et al teach complexes formed between two binding members, and the x-ray crystallography of Fesik et al is performed on complexes between two binding members.

With regards to claim 31, Ullman et al teach that a specific binding partner member can be attached to the photosensitizer through a particle (i.e. linker). See column 42, lines 17-19.

11. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Starling et al (US 6,372,215 B1).

Ullman et al reference has been disclosed above and additionally teaches that the assay can be performed competitively by combining a sample (i.e. test biomolecule) and a specific binding pair member linked to a photosensitizer (i.e. sensitizer-linked substrate molecule) and then adding analyte analog (i.e. candidate agent). See column 37, lines 25-28 and column 42, lines 17-19.

However, Ullman et al fail to teach that a plurality of candidate agents are added and also fail to teach the step of selecting the identifying agent based on the modulating capacity of each of the candidate agents.

Starling et al reference teaches the step of performing high throughput screening assays by providing competitor test binding agents from a library of peptides and small molecules, in order to identify and characterize additional agents that can bind to a target species, wherein the additional agents can be applied as diagnostic and therapeutic agents for inflammatory or autoimmune diseases. See column 3, lines 17-35 and column 15, line 57 to column 17, line 2.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al with the step of performing high throughput screening assays by providing competitor test binding agents from a library of peptides and small molecules, as taught by Starling et al, with the expected benefit of identifying and characterizing additional agents that can bind to a target species, wherein the additional agents can be applied as diagnostic and therapeutic agents for inflammatory or autoimmune diseases. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including

high throughput screening of competitor test binding agents, as taught by Starling et al, in the method of Ullman et al, since Ullman et al also teach competitive assays.

12. Claims 23-25, 33, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 20 above, and further in view of Gelboin et al (US 6,060,253).

Ullman et al and Fesik et al references have been disclosed above, but fail to teach that the target biomolecule is cytochrome P450.

Gelboin et al teach cytochrome P450 enzyme as an analyte in an immunoassay, in order to identify enzymes that metabolize drugs or a carcinogen. See column 1, lines 10-28 and column 12, lines 15-28.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al and Fesik et al with cytochrome P450 enzyme as an analyte in an immunoassay, as taught by Gelboin et al, with the expected benefit of identifying enzymes that metabolize drugs or a carcinogen. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including cytochrome P450 as a target biomolecule, as taught by Gelboin et al, in the method of Ullman et al and Fesik et al, since Ullman et al and Fesik et al teach immunoassays to detect a target biomolecule, and the cytochrome P450 of Gelboin et al is one type of biomolecule that can be detected in an immunoassay.

13. Claims 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 26 above, and further in view of Ullman et al (US 6,406,913 B1).

Ullman et al and Fesik et al references have been disclosed above, but fail to teach that the photosensitizer is $Ru(bpy)_3^{2+}$.

Ullman et al teach $Ru(bpy)_3^{2+}$, in order to provide a dye that has high fluorescent quantum yields. See column 28, lines 40-45.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al ('581) and Fesik et al with $Ru(bpy)_3^{2+}$, as taught by Ullman et al ('913), with the expected benefit of providing a dye that has high fluorescent quantum yields. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including $Ru(bpy)_3^{2+}$, as taught by Ullman et al ('913), in the method of Ullman et al ('581) and Fesik et al, since Ullman et al ('581) and Fesik et al teach photosensitizers in assays, and the $Ru(bpy)_3^{2+}$ of Ullman et al ('913) is one type of sensitizer that can be used in an assay.

14. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 26 above, and further in view of Barton (US 5,157,032).

Ullman et al and Fesik et al references have been disclosed above, but fail to teach that said photosensitizer is $[Ru(phen)_2(dppz)]^{2+}$.

Barton reference teaches $[Ru(phen)_2(dppz)]^{2+}$, in order to provide a non-radioactive luminescent DNA probe for assay systems. See column 45, lines 12-21.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al and Fesik et al with $Ru(phen)_2(dppz)]^{2+}$, as taught by Barton, with the expected benefit of providing a non-radioactive luminescent DNA probe for assay systems. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including $Ru(phen)_2(dppz)]^{2+}$, as taught by Barton, in the method of Ullman et al and Fesik et al, since Ullman et al and Fesik et al teach labels for assays, and the $Ru(phen)_2(dppz)]^{2+}$ of Barton is one type of label that can be used in an assay.

15. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 26 above, and further in view of Wang et al (US 5,696,157).

Ullman et al and Fesik et al been disclosed above, but fail to teach that the photosensitizer is a 7-coumarin molecule.

Wang et al teach a 7-aminocoumarin as a fluorescent label to prepare fluorogenic substrates for enzymes, in order to provide excitation in the ultraviolet and blue to blue-green emission spectra. See column 1, lines 20-32.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al and Fesik et al with a 7-aminocoumarin as a fluorescent label to prepare fluorogenic substrates for enzymes, as taught by Wang

et al, with the expected benefit of providing excitation in the ultraviolet and blue to blue-green emission spectra. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a 7-aminocoumarin, as taught by Wang et al, in the method of Ullman et al and Fesik et al, since Ullman et al and Fesik et al teach labeling of receptors, and the 7-aminocoumarin of Wang et al is capable of labeling enzyme substrates, which is a type of receptor.

16. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 20 above, and further in view of Goodbody et al (US 5,569,745).

Ullman et al and Fesik et al references have been disclosed above, but fail to teach that said linker is an alkyl chain, $(CH_2)_n$, wherein n = 1-13.

Goodbody et al teach an alkyl chain, in order to couple two compounds without adversely affecting the functions of either compound. See column 4, lines 24-33.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al and Fesik et al with an alkyl chain, as taught by Goodbody et al, with the expected benefit of coupling two compounds without adversely affecting the functions of either compound. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including an alkyl chain, as taught by Goodbody et al, in the method of Ullman et al and Fesik et al, since Ullman et al and Fesik et al teach conjugates of biological molecules and particles, and the alkyl chain of Goodbody et al is linked between a peptide and metal

chelate, which is an example of a conjugation between a biological molecule and a particle.

17. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 20 above, and further in view of Gelboin et al (US 6,060,253) as applied to claims 33 above, and in further view of Thirugnanam (US 5,506,251).

Ullman et al, Fesik et al, and Gelboin et al references have been disclosed above, but fail to teach that said substrate is imidazole.

Thirugnanam reference teaches imidazole, in order to provide a cytochrome p450 inhibitor. See column 1, lines 35-43.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al, Fesik et al, and Gelboin et al with teaches imidazole, as taught by Thirugnanam, with the expected benefit of providing a cytochrome p450 inhibitor. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including imidazole, as taught by Thirugnanam, in the method of Ullman et al, Fesik et al, and Gelboin et al, since Ullman et al, Fesik et al, and Gelboin et al teach substrates that bind to cytochrome P450, and the imidazole of Thirugnanam is one type of substrate that can bind to cytochrome P450.

18. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ullman et al (US 6,251,581 B1) in view of Fesik et al (US 5,698,401) as applied to claim 26 above, and further in view of Leung et al (Bioorganic & Medicinal Chemistry Letters, 1999).

Ullman et al and Fesik et al references have been disclosed above, but fail to teach that the photosensitizer is a 7-, substituted coumarin molecule conjugated to nitric oxide synthase.

Leung et al teach a 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid fluorescent dye, in order to enhance fluorescence quantum yields. See page 2230, 1st paragraph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Ullman et al and Fesik et al with a 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid fluorescent dye, as taught by Leung et al, with the expected benefit of enhancing fluorescence quantum yields. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid fluorescent dye, as taught by Leung et al, in the method of Ullman et al and Fesik et al, since Ullman et al and Fesik et al teach labeling of biomolecule substrate with fluorescent dyes, and the 7-amino-4-methyl-6-sulfocoumarin-3-acetic acid fluorescent dye of Leung et al is one type of fluorescent dye.

Allowable Subject Matter

19. Claim 36 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20. The following is a statement of reasons for the indication of allowable subject matter: Claim 36 is directed to structures of a conjugate, wherein the conjugate is a dipeptide amide linked to a specific coumarin molecule, and wherein the coumarin label and dipeptide amide are attached through a linker. The prior does not teach the claimed structures. The prior art does teach coumarin molecules linked to structures that include the dipeptide amide structure, but the specific linking structure claimed is not taught by the prior art as linking the coumarin molecules and dipeptide amide.

21. Claims 38-45 and 47 are allowed for the same reason give above with respect to claim 36.

Response to Arguments

22. On pages 9-10 of the Remarks, filed 03 August 2005, Applicants stated that a new declaration was filed on May 2, 2002. However, there is no record of the said

declaration in the file. With regards to the PTO-issued Notice of Acceptance on July 11, 2002 and Applicants' statement that "all the items in the application were acceptable", this notice does not indicate whether the declaration is proper, but simply that a declaration has been submitted. Therefore, the requirement for Applicants to supply a proper declaration per the previous Office Action is maintained.

23. Amended claims 21-22 have overcome the previously applied rejections under 35 U.S.C. 112, 2nd paragraph, and Applicant's arguments regarding the rejection of claim 28, as stated on page 10 of the Remarks, has been found persuasive. The previously applied rejection under 35 U.S.C. 112, 2nd paragraph of claim 28 has been withdrawn.

24. Applicant's arguments with respect to claims 20-35 on pages 11-19 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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11/11/05